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## Assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): Venezuelan equine encephalitis

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## Assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): Venezuelan equine encephalitis

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### Abstract

Venezuelan equine encephalitis (VEE) has been assessed according to the criteria of the Animal Health Law (AHL), in particular criteria of Article 7 on disease profile and impacts, Article 5 on the eligibility of VEE to be listed, Article 9 for the categorisation of VEE according to disease prevention and control rules as in Annex IV and Article 8 on the list of animal species related to VEE. The assessment has been performed following a methodology composed of information collection and compilation, expert judgement on each criterion at individual and, if no consensus was reached before, also at collective level. The output is composed of the categorical answer, and for the questions where no consensus was reached, the different supporting views are reported. Details on the methodology used for this assessment are explained in a separate opinion. According to the assessment performed, it is inconclusive whether VEE is eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL because there was no full consensus on the criterion 5 A(v). Consequently, since it is inconclusive whether VEE can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, the assessment on compliance of VEE with the criteria as in Sections 4 and 5 of Annex IV to the AHL, for the application of the disease prevention and control rules referred to in points (d) and (e) of Article 9(1), and which animal species can be considered to be listed for VEE according to Article 8(3) of the AHL is also inconclusive.

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**Keywords:** Venezuelan equine encephalitis, VEE, Animal Health Law, listing, categorisation, impact

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## 1. Introduction

### 1.1. Background and Terms of Reference as provided by the requestor

The background and Terms of Reference (ToR) as provided by the European Commission for the present document are reported in Section 1.2 of the scientific opinion on the ad hoc methodology followed for the assessment of the disease to be listed and categorised according to the criteria of Article 5, Annex IV according to Article 9, and 8 within the Animal Health Law (AHL) framework (EFSA AHAW Panel, 2017).

### 1.2. Interpretation of the Terms of Reference

The interpretation of the ToR is as in Section 1.2 of the scientific opinion on the ad hoc methodology followed for the assessment of the disease to be listed and categorised according to the criteria of Article 5, Annex IV according to Article 9, and 8 within the AHL framework (EFSA AHAW Panel, 2017).

The present document reports the results of assessment on Venezuelan equine encephalitis (VEE) according to the criteria of the AHL articles as follows:

- Article 7: Venezuelan equine encephalitis profile and impacts
- Article 5: eligibility of Venezuelan equine encephalitis to be listed
- Article 9: categorisation of Venezuelan equine encephalitis according to disease prevention and control rules as in Annex IV
- Article 8: list of animal species related to Venezuelan equine encephalitis.

## 2. Data and methodologies

The methodology applied in this opinion is described in detail in a dedicated document about the ad hoc method developed for assessing any animal disease for the listing and categorisation of diseases within the AHL framework (EFSA AHAW Panel, 2017).

## 3. Assessment

### 3.1. Assessment according to Article 7 criteria

This section presents the assessment of VEE according to the Article 7 criteria of the AHL and related parameters (see table 2 of the opinion on methodology (EFSA AHAW Panel, 2017)), based on the information contained in the fact-sheet as drafted by the selected disease scientist (see Section 2.1 of the scientific opinion on the ad hoc methodology) and amended by the AHAW Panel.

#### 3.1.1. Article 7(a) Disease Profile

VEE is caused by infection with the VEE virus (VEEV) from the *Togaviridae* family, the *Alphavirus* genus and species *Venezuelan equine encephalitis virus*. There are at least 14 subtypes and varieties within the VEE complex but only subtype I, varieties AB and C have been associated with major equine epizootics and epidemics (Aguilar et al., 2011). The IA and IB strains are considered genetically indistinguishable and are thus classified as IAB.

VEEV can cause very high morbidity in humans and equines with a case-fatality rate of 50–70% in horses and less than 1% in humans. Domestic rabbits, goats, dogs and sheep are also potentially susceptible animals. Transmission occurs by the bite of an infected mosquito.

##### 3.1.1.1. Article 7(a)(i) Animal species concerned by the disease

There are two types of cycles involved in VEEV. The enzootic cycle is maintained by rodents and mosquitoes. Wild rodents (*Sigmodon* spp., *Proechimys* spp., *Peromyscus* spp., *Oryzomys* spp., *Zygodontomys* spp. and *Heteromys* spp.) are the main reservoirs during enzootic circulation although bats and opossum (*Didelphis marsupialis*) could maintain the sylvatic cycle. Birds may also be involved. Horses do not seem to be efficient amplifying hosts for any enzootic VEEVs (OPS-OMS, 2003; Carrara et al., 2005; Mesa et al., 2005; Thompson et al., 2015).

Current knowledge suggests that the epizootic strains emerge from genetic modification of enzootic strains (OIE, 2013b). The epizootic cycle implicates horses, mosquitoes and humans, although there is the potential for the virus to affect many other animal species. Equidae serve as amplifying hosts for

epizootic VEEV strains; horses and donkeys produce high viraemia which in turn infect a wide range of mosquitoes (OIE, 2013b). Humans are susceptible to infection when epizootic cycles occur: normally humans are considered incidental or dead-end hosts but they could play a role as maintenance and amplifying hosts due to the high viraemic titres (Aguilar et al., 2004; Quiroz et al., 2009). Other animals can be infected but there is no evidence that VEEV strains are maintained in rodents or other animals between epidemics.

A number of animal species have been experimentally infected including equines (Walton et al., 1973; Sahu et al., 2003), rabbits (Bowen, 1976), rodents (Carrara et al., 2005, 2007; Deardorff et al., 2009), pigs, cattle (Dickerman et al., 1973) and macaques (Danes et al., 1973a; Reed et al., 2004). Cattle, swine, chickens and dogs have been shown to seroconvert after epizootics and infections have also been reported in mammals such as pigs, cattle, goats, sheep, dogs, rabbits and some birds (de La Monte et al., 1985).

### 3.1.1.2. Article 7(a)(ii) The morbidity and mortality rates of the disease in animal populations

A serological survey carried out in 2001 in Mexico concluded that rodent reservoir hosts in endemic areas seem to be clinically unaffected; however, other wild and laboratory (or pet) rodents can become ill when infected by VEEV. Mice and hamsters are generally more susceptible than guinea pigs. Enzootic strains are not known to cause any illness in equids, other domesticated livestock, dogs or cats, with the exception of one Mexican I-E variant, which is pathogenic for equids (Ulloa et al., 2003). Epizootic strains from subtypes IAB and IC are highly pathogenic for horses, with reported case-fatality rates of between 20% and 80%. Recent surveys demonstrated that cattle, swine, chickens and dogs have been shown to seroconvert after epizootics; and mortality has been observed in domesticated rabbits, dogs, goats and sheep (Weaver et al., 2004; Mesa et al., 2005; Zacks and Paessler, 2010; FAD-PRP/USDA, 2013; CFSPH, 2015; OIE, 2013b).

Equine morbidity and mortality rates from epizootic outbreaks vary widely and are estimated to be from 10% to 100% and 20% to 80%, respectively. Enzootic VEEV almost never causes disease or fatalities in equids.

Data about seroprevalence studied in different groups of animals are available. In Costa Rica, the seroprevalence in two-toed sloths (*Choloepus* spp.) was 11%; in Mexico, the seroprevalence in cattle was 45%, in Trinidad, the seroprevalence in horses was 0.8% for samples taken between 2006 and 2009 (Thompson et al., 2012) and in bats it was 2.9% (2006–2008) (Thompson et al., 2015).

Another study carried out in Mexico, between 2003 and 2004 found 17%, 72% and 52% seropositive horses in the States Tamaulipas, Veracruz and Tabasco, respectively. Testing 'hots-spots' in a later study in between 2008 and 2010 in the State Veracruz (the region where VEEV was circulating most actively in the previous study) resulted in a seroprevalence of 100% in horses and bovids; in all rodents tested in 2008–2009, a seroprevalence of 83%, in Chapman's rice rat (*Handleyomys chapmani*) 25%, and in Toltec cotton rat (*Sigmodon toltecus*) 30% (38/126) (Adams et al., 2012). It should be noted that the sampling strategy in these surveys reported by Adams et al. (2012) has not been documented.

In 1969, the virus caused 20,000 equine deaths in Ecuador and 50,000 in Mexico. In Texas, between June and August of 1971, 2,000 infected horses were reported with 1,426 associated deaths. In 1992, 4,000 equine deaths were reported caused by VEEV in Venezuela and Colombia (Aguilar et al., 2011).

### 3.1.1.3. Article 7(a)(iii) The zoonotic character of the disease

#### Presence

#### Parameter 1 – Report of zoonotic human cases (anywhere)

VEEV is zoonotic. It is spread between horses and humans via mosquitoes. In the 1960s, over 200,000 human cases and 100,000 equine deaths were reported in Colombia and smaller epidemics occurred in Venezuela and Mexico. Between 75,000 and 100,000 human cases and about 4000 equine deaths were reported in Venezuela and Colombia in 1995 (Aguilar et al., 2011). A randomised household illness and antibody survey of 681 Port Isabel residents revealed an overall antibody prevalence of 3.2% in humans (Bowen and Calisher, 1976).

In humans, VEE is usually an acute, often mild, systemic illness (CFSPH, 2015). Symptoms are similar to the ones reported for horses: mild to severe influenza-like symptoms (headache, fatigue, myalgia, nausea, vomiting, pharyngitis) (Weaver et al., 2004).



Human morbidity rates are extremely high (90–100%), but fatalities are rare and seen in less than 1% of cases and severe neurological signs are reported in 4–14% of infections (FAD-PRP/USDA, 2013). More severe illness and higher mortality rates are observed in children and the elderly (FAD-PRP/USDA, 2013; CFSPH, 2015).

#### **3.1.1.4. Article 7(a)(iv) The resistance to treatments, including antimicrobial resistance**

##### **Parameter 1 – Resistant strain to any treatment even at laboratory level**

No treatments have been described for VEEV infection. Supportive treatment may be given to alleviate symptoms.

Some experimental assays show possible effects against VEEV of pegylated alpha interferon, carbodine and interfering RNAs but more data are needed (Lukaszewski and Brooks, 2000; O'Brien, 2007; Julander et al., 2008).

#### **3.1.1.5. Article 7(a)(v) The persistence of the disease in an animal population or the environment**

Animals are infectious during the viraemic period, as determined through experimental infection of some species as described below.

The incubation period in horses is about 5–14 days. The first detection of the virus in blood after inoculation can vary from 1 to 4 days in horses (Walton et al., 1973; Justines et al., 1981; Wang et al., 2001; Gonzalez-Salazar et al., 2003; Greene et al., 2005).

Titres of 4–5 log of LD<sub>50</sub> have been observed in the blood of an infected hispid cotton rat (*Sigmodon hispidus*) for 5 days and viruria was observed for 2–8 days (Zarate and Scherer, 1968; Howard, 1974). Virus has been detected in throat swabs from spiny rats (*Proechimys* spp.) experimentally infected (Yound and Johnson, 1969; Carrara et al., 2005).

Birds develop moderate viraemia for 2–3 days (Chamberlain et al., 1956; Grayson and Galindo, 1968; Aitken et al., 1969).

Antibodies against VEEV have been detected in bats although there are insufficient data about a possible role of bats in VEEV transmission (Thompson et al., 2015).

Experiments have demonstrated that infected mosquitoes can be stored at 4°C for 7 days without loss of infectivity, although 2 days at 22°C produced complete loss of infectivity (Andrews and Turell, 2016). While the common rule is that Togaviruses can be inactivated by 15 min at 65°C, it has been shown that three different alphaviruses (Ross River, Barmah Forest and O'nyong'nyong viruses) need specific parameters for complete heat inactivation so the inactivation conditions should be established specifically for VEEV (PHAC, 2011). Like other enveloped viruses, the VEEV is susceptible to disinfectants such as 1% sodium hypochlorite, 4% formaldehyde, 2% glutaraldehyde, 70% ethanol and 3–6% hydrogen peroxide. Alphavirus virions are stable at pH 7–8. They are susceptible to radiant sunlight, moist or dry heat and drying thus cool, moist, dark conditions favour survival (OIE, 2013b; PHAC, 2011).

The virus can persist in dried blood or exudates and it has been demonstrated that it can last 98 h on a glass surface at room temperature in the dark (Sagripanti et al., 2010).

#### **3.1.1.6. Article 7(a)(vi) The routes and speed of transmission of the disease between animals, and, when relevant, between animals and humans**

The main route of VEEV transmission is through the bite of an infected mosquito. *Psorophora columbiae*, *Psorophora confinnis*, *Aedes sollicitans*, *Aedes taeniorhynchus*, *Mansonia indubitans* and *Deinocerites pseudus* are vectors for epizootic VEEV, while *Culex (Melanoconion)* species seem to be the main vector for enzootic strains (Aitken et al., 1969; Ferro et al., 2003; Aguilar et al., 2011). The mosquitoes species in which VEEV has been detected and occurring in the European Union (EU) are listed in (EFSA AHAW Panel, 2017). Transovarial transmission has not been proved.

Aerosol, subcutaneous injection, nasal instillation and contact with broken skin or contaminated animal bedding are also ways to spread the virus (Zarate and Scherer, 1968; Danes et al., 1973b; Reed et al., 2004); so, while the main route of transmission is by infected mosquitoes, VEEV is highly infectious as an aerosol. Mechanical transmission of epizootic VEEV has been demonstrated for blackflies (*Simulium* spp.) (Homan et al., 1985). Horse to human and human to human transmission has not been recorded. No contact transmission experiments have been found and transplacental infection has not been reported.

### 3.1.1.7. Article 7(a)(vii) The absence or presence and distribution of the disease in the Union, and, where the disease is not present in the Union, the risk of its introduction into the Union

Sporadic cases of infection by VEEV occur in endemic regions although it can cause outbreaks or epidemics when susceptible animals or humans, infected mosquitoes and selected subtypes of viruses coincide. As for other arboviruses exotic in EU, the occurrence of sporadic cases, outbreaks or epidemics depends on the control activities carried out if the virus enters into the territory.

VEEV is not present in the EU. The virus is widely distributed through South and Central America and, in spite of the presence of low virulence strains of the virus in southern Florida, it is considered exotic in USA. It is also considered exotic in Canada and Europe (Aguilar et al., 2011; CFSPH, 2015).

The risk of entry of VEEV into Europe is through infected mosquitoes, rodents, birds, horses and humans. Establishment and apparition of cases because of VEEV infection has been estimated as moderate to high, with Belgium, the south of England and the north of Italy being the places in Europe where the possibility of VEEV cases is higher (Pfeffer and Dobler, 2010; Durand et al., 2013).

The number of animals considered as potential hosts for VEEV that have been imported into Europe between 2005 and 2009 is shown in the Table 1 (number of animal imports and consignments (in brackets)). The main risk for introduction and infection of local mosquitoes is through horses and during this period, none of the imported animals originated from a country that had reported clinical cases in that period (Durand et al., 2013).

**Table 1:** Number of potential hosts for VEEV and number of consignments imported into Europe (2005–2009) (Extracted from Durand et al. (2013), data from TRACES)

Species	Origin of the animals, number (consignments)	
	North America	South America
Horses	–	15,703 (2,025)
Birds	391,348 (169)	49,209 (160)
Rodents	215,780 (5,879)	448 (11)

The duration of the infectious period depends on the duration and level of viraemia and some of these data are shown in Section 3.1.1.5.

As a general rule, to avoid the entry of infected animals, Equidae must come from third countries which have been free for at least 2 years from VEE.<sup>1</sup>

### 3.1.1.8. Article 7(a)(viii) The existence of diagnostic and disease control tools

Acute neurological signs can lead to a presumptive diagnosis of equine encephalomyelitis during the summer in temperate climates or in the wet season in tropical or subtropical climates, when haematophagous insects are active. Confirmation of the diagnosis of VEEV infection can be carried out by virus isolation (in cell cultures or in laboratory animals) and subsequent identification, and antigenic classification of the isolated virus.

VEEV can be identified by polymerase chain reaction (PCR), complement fixation (CF), haemagglutination inhibition (HI), plaque reduction neutralisation (PRN) or immunofluorescence tests using VEE-specific antibodies. After infection, PRN antibodies appear within 5–7 days, CF antibodies within 6–9 days, and HI antibodies within 6–7 days.

For direct detection, blood or serum of febrile animals or brain tissue of encephalitic animals in an early stage of infection could be used. Viraemia terminates 5–6 days after infection, and coincides with the production of neutralising antibodies and the appearance of clinical neurological signs. As for other arboviruses, the period of viraemia is short and the titre is low so PCR and/or viral isolation could be useful only if the sample was taken in acute phases of the disease and cold chain is well preserved. Isolates may sometimes be obtained from CSF or from brain tissue (either at necropsy or post-mortem needle biopsy). Direct detection (and identification) of the virus confirms its presence.

Detection of IgM in CSF samples could also be confirmatory although infection by other alphaviruses should be ruled out by epidemiological criteria and/or laboratory discrimination of the presence of antigenically related alphaviruses. Virus-neutralisation technique is needed to do that. If

<sup>1</sup> Council Directive 2009/156/EC of 30 November 2009 on animal health conditions governing the movement and importation from third countries of Equidae. OJ L 192, 23.7.2010, p. 1–24.



no CSF is available and only serum samples are available, two samples taken at least 7 days apart are required to see a four-fold rise in the antibodies titre against VEEV.

Previous vaccination can also interfere with interpretation of results, so a detailed clinical history and two paired sera samples and/or CSF for IgM or direct detection are needed although demonstration of VEE-specific serum IgM antibodies in a single serum sample supports recent virus exposure (OPS-OMS, 2003; Mesa et al., 2005; OIE, 2013a,b).

As for other mosquito borne viruses, control of infection is by control of the mosquito vector mainly by elimination of mosquito breeding locations (i.e. pooled or stagnant water). The other prevention method is through the amplifier host in epidemics, through quarantine and movement controls of all Equidae, vaccination of equids, stabling horses in screened housing; especially during prime daily mosquito activity and using repellents (OIE, 2013b).

A modified live vaccine (MLV) has been widely used against VEEV. It is derived from the Trinidad donkey strain (variant IAB) that was attenuated by two point mutations after passage in guinea-pig heart cells. It induces protective and durable immunity in horses but may also cause adverse effects in horses and humans. Its use is controversial because of residual neurovirulence and the potential to revert into a virulent strain. Inactivated vaccines have also been developed but they require the growth of large quantities of virus and possible adverse effects due to incomplete inactivation in the case of virulent strains. Currently, the only available VEEV vaccines for equids in the USA are killed products using the attenuated strain that are available in different combinations with vaccines against Eastern and Western Equine Encephalitis (EEE and WEE) and other equine diseases. A MLV would likely be conditionally released in the face of an outbreak.

Human vaccination is only recommended for laboratory workers and for military personnel. Vaccination against VEE in horses is controversial. As with other exotic diseases, the presence of vaccination derived antibodies may complicate serological detection during an outbreak. Further, core vaccination against EEE and WEE could protect from VEE and in the event of an outbreak, vaccination with the highly effective MLV product would induce rapid, complete immunity while allowing for accurate surveillance before VEE specific vaccination. To date in the US, the use of killed VEE vaccine is only recommended in high-risk areas (OPS-OMS, 2003; Mesa et al., 2005; AAEP, 2015; Arechiga-Ceballos and Aguilar-Setien, 2015; OIE, 2013b).

New approaches based on recombinants with viruses like Vaccinia, Sindbis or Baculovirus are under investigation (Minke et al., 2004).

### **3.1.2. Article 7(b) The impact of diseases**

#### **3.1.2.1. Article 7(b)(i) The impact of the disease on agricultural and aquaculture production and other parts of the economy**

VEE is not present in Europe. The economic impact for horses is not well established. In places where Equidae are important for agriculture and transportation, this disease remains important. It is considered the most important New World alphaviral disease (Weaver, 2001).

#### **3.1.2.2. Article 7(b)(ii) The impact of the disease on human health**

No transmission between humans has been described and a mosquito is essential to transmit the virus from animals to humans.

VEE in humans can be associated with nonlethal, nonspecific, incapacitating illness in which fever, headache, malaise, myalgia, sore throat and vomiting are the most common features. Lymphopenia and elevated hepatic enzymes are commonly seen during acute illness. It seems that between 0.1% and 7% of dengue-like illness in Latin America is caused by VEEV (Aguilar et al., 2011). An inapparent infection ratio of 1:11 has been reported (Franck and Johnson, 1971; Bowen and Calisher, 1976), where a randomised household illness and antibody survey of 681 Port Isabel residents revealed an overall antibody prevalence of 3.2% (Bowen and Calisher, 1976) and only in a small percentage of natural cases of VEE (0.5% of adults and up to 4% of children) is central nervous system (CNS) infection apparent. In these cases, CNS involvement involves a second phase of disease after a few days from the acute febrile phase. The severity of neurological disease ranges from somnolence and mild confusion to seizures, ataxia, paralysis and coma. Mortality in neurological cases is as high as 35% in children and 10% in adults (Bowen et al., 1976). Long-term neurological deficits, abortions and teratogenic effects have also been reported due to VEEV. The virus has been recovered from brains of aborted fetuses or stillborns. An increase in the number of spontaneous abortions was detected when compared with prior years and a pregnant woman who was vaccinated with the TC-383

VEEV vaccine suffered the loss of her foetus (Casamassima et al., 1987; Weaver et al., 1996; Rivas et al., 1997). In addition, a fulminant lethal form of VEE with a short clinical course and extensive lymphoid damage, and little or no evidence of CNS infection, has been described (Johnson et al., 1968). Humans are susceptible to aerosolised virus and this has been reflected as a high number of laboratory-acquired infections involving VEEV aerosols (Hanson et al., 1967).

In 1971, VEEV caused an outbreak in Texas, with 86 hospital-based surveillance cases. Forty-eight of the 86 cases reported follow up 9 months to 1 year after recovery. Of these, 12 cases were confirmed to present with long-lasting neurological sequelae occurring months after the clearance of the acute infection. In these cases, the sequelae included paralysis, reductions in hearing, taste and smell, and headaches, fatigue and depression can occur (Bowen et al., 1976). In 1995, in Columbia, 75,000 people were infected, 300 died and 3,000 suffered neurological complications. Seizures and neuropsychological changes were common among those with neurological complications (Rivas et al., 1997). More recently, in 2010, a VEEV outbreak occurred alongside EEEV in Panama, during which 11 confirmed cases of VEE were reported, including four with long-term sequelae. These patients spent less than 1 week in the hospital, but three patients suffered altered mental status and one experienced seizures (Carrera et al., 2013). In spite of VEE being historically underreported, it cannot be ruled out as a large contributor to human encephalitic disease with resultant sequelae.

Neurological sequelae (convulsions, somnolence, confusion, photophobia, coma, intellectual disability, and emotional instability/behavioural changes) have been described in 4–14% of the survivors after VEE (Ronca et al., 2016). As previously specified, there is no specific treatment. Currently, no vaccines have been authorised for use in the EU by the European Medicine Agency (EMA, 2017).

### **3.1.2.3. Article 7(b)(iii) The impact of the disease on animal welfare**

#### **Parameter 1 – Severity of clinical signs at case level and related level and duration of impairment**

As reported in the literature, only equine and human populations are affected by disease caused by this virus, although mortality has been observed in domesticated rabbits, dogs, goats and sheep (Weaver et al., 2004; Zacks and Paessler, 2010; OIE, 2013b).

Clinical disease in equids may vary from very mild signs of fever, anorexia and depression to encephalitis signs and sometimes death. Subclinical infection is most often associated with enzootic strains of VEE. Moderate illness is characterised by inappetence, pyrexia and depression associated to fever. A severe but non-fatal presentation is associated to continued anorexia and high fevers, with tachycardia and depression progressing to more severe central nervous system involvement including paresis, muscle fasciculation and spasms, incoordination, staggering, ataxia resulting in open stance to prevent falling, head pressing, bruxism, circling or rocking on limbs, paddling in animals which have fallen or are in lateral recumbency, stupor and/or convulsions often resulting in permanent neurologic damage. Finally, this severe illness can be fatal. Death can be sudden or occur within hours from the onset of neurological signs (CFSPH, 2015).

### **3.1.2.4. Article 7(b)(iv) The impact of the disease on biodiversity and the environment**

Many rodents and other animals could potentially be infected by these viruses, even though mainly equines are affected. Mortality in wild species has not been observed.

The virus can persist in dried blood or exudates and it has been demonstrated that it can last 98 h on a glass surface at room temperature in the dark (Sagripanti et al., 2010).

### **3.1.3. Article 7(c) Its potential to generate a crisis situation and its potential use in bioterrorism**

VEEV is listed in the OIE list of notifiable terrestrial and aquatic animal diseases (OIE, 2016b). It is also included in the List of Human and Animal Pathogens and Toxins for Export Control by the Australia group (AG, 2016). It is classified in the category B (viral encephalitis (alphaviruses (e.g. VEE, EEE, WEE)) of CDC Bioterrorism Agents (CDC, online-a). Subtypes IAB and IC are considered as 'select agents' by the CDC meaning that they have the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal or plant products (CDC, online-b). While not naturally transmitted as an aerosol, VEEV is highly infectious and is easily produced in this form in large quantities. For this reason, the virus had been developed as a biological weapon by the United States during the Cold War and the Soviet biological weapons program also researched and weaponised VEEV (Croddy et al., 2002).

### **3.1.4. Article 7(d) The feasibility, availability and effectiveness of the disease prevention and control measures**

#### **3.1.4.1. Article 7(d)(i) Diagnostic tools and capacities**

There are no commercial or officially or internationally recognised methods for VEEV diagnosis. The Se and Sp of the available methods have not been determined. The European expert laboratory network for emerging viral diseases (EVD-Labnet) reported 10 European countries (Denmark, France, Germany, Italy, Luxembourg, Slovenia, Switzerland, The Netherlands, Spain and the UK), where specific detection of VEEV could be conducted (EVD-Labnet, 2017). Samples for accurate diagnosis include CSF, serum/blood or other tissues for direct detection and serum for serology.

#### **3.1.4.2. Article 7(d)(ii) Vaccination**

Vaccines based on inactivation of wild-type VEEV were used in the past but their use ceased because of incomplete inactivation resulting in several epidemics (Brault et al., 2001). In endemic regions in South America, vaccination of equids is carried out using a live attenuated strain (TC-83) developed from a wild type IAB strain with two effective attenuating mutations (Minke et al., 2004). The TC-83 vaccine produces long lasting neutralising antibodies: after one month of vaccination, 87% of the horses had developed VEE-neutralising (Nt) antibodies and one year later 73% had VEE Nt antibodies (Ferguson et al., 1978).

However, the vaccine is reactogenic, it could revert to wild-type, be spread by mosquitoes and does not seem to protect against enzootic viruses (Pedersen et al., 1972; Kinney et al., 1993; Pittman et al., 1996). To solve these problems, formalin-inactivated TC-83 is used in USA (Minke et al., 2004; Aguilar et al., 2011). But the formalin-inactivated TC83 used in USA, as most of inactivated vaccines, confers short-lived immunity only and frequent boosters are required (Aguilar et al., 2011; AAEP, 2015).

According to the OIE, the attenuated vaccine is used as a single dose in animals over 3 months, and the inactivated vaccine is administered in two doses with an interval of 2–4 weeks between doses.

Other approaches used to obtain a vaccine are based on Vaccinia, Baculovirus or Sindbis recombinants or full-length cDNA clones containing attenuating mutations (Minke et al., 2004). Recently, an IRES-based VEE vaccine candidate based up the IE serotype was shown to offer complete protection against a lethal subtype IE VEEV challenge in mice and against febrile disease in cynomolgus macaques showing good indicators of safety and efficacy (Rossi et al., 2015).

No vaccines have been authorised for use in EU by the European Medicine Agency (EMA, 2017).

#### **3.1.4.3. Article 7(d)(iii) Medical treatments**

There are no medical treatments specific for VEEV available.

#### **3.1.4.4. Article 7(d)(iv) Biosecurity measures**

Good biosecurity consists of simple measures to control the mosquito vector and protocols designed to minimise the exposure of horses to disease-causing agents and vectors through quarantine and movement controls of all Equidae, vaccination of equids, stabling horses in screened housing; especially during prime daily mosquito activity and using repellents (OIE, 2013b). These biosecurity practices will reduce the risk of disease transmission between horses both at their home stables and when competing at events but no specific guidelines for VEEV have been found.

#### **3.1.4.5. Article 7(d)(v) Restrictions on the movement of animals and products**

Currently, no specific measures are laid down in the EU legislation for VEEV outbreak control and the EU does not apply any specific trade restrictions to prevent import of VEEV.

In the Americas, movement of equids from infected regions to free areas is controlled within affected countries and in frontiers with other countries (Mesa et al., 2005; FAD-PRReP/USDA, 2013) although in some cases, such as in some areas in the frontier between Venezuela and Colombia, it is difficult due mainly to clandestine transboundary movement of people and animals.

Vaccination status could be requested from the original country and quarantine period should be established in the country of origin and/or destination. Veterinary Authorities of VEE free countries may prohibit imports or transits through their territory, from countries considered infected with VEE, of domestic and wild equines, and may prohibit the importation into their territory, from countries considered infected with VEE, of semen and embryos/ova of domestic and wild equines (OIE, 2010).

The recommendations in the terrestrial code of the OIE for import of domestic and wild equines from free countries (OIE, 2010) are that the Veterinary Authorities of importing countries should require the presentation of an international veterinary certificate attesting that the animals:

- 1) showed no clinical sign of VEE on the day of shipment;
- 2) have not, during the past six months, been in any country in which VEE has occurred in the last two years; and
- 3) have not been vaccinated against VEE within 60 days prior to shipment.

The recommendations for importation of domestic and wild equines from VEE infected countries (OIE, 2010) are that the Veterinary Authorities of importing countries should require the presentation of an international veterinary certificate attesting that the animals:

- 1) vaccinated animals:
  - a. were vaccinated against VEE not less than 60 days prior to shipment and were clearly identified with a permanent mark at the time of vaccination;
  - b. were kept in a quarantine station in the country of origin under official veterinary supervision for three weeks prior to shipment and remained clinically healthy during that period; any animal which showed a rise in temperature (taken daily) was subjected to a blood test for virus isolation, with negative results;
  - c. were protected from insect vectors during transportation to and from the quarantine station and during the quarantine period; and
  - d. showed no clinical sign of VEE on the day of shipment;
- 2) unvaccinated animals:
  - a. were kept in a quarantine station in the country of origin under official veterinary supervision for 3 weeks prior to shipment and remained clinically healthy during that period; any animal which showed a rise in temperature (taken daily) was subjected to a blood test for virus isolation, with negative results;
  - b. were subjected to a diagnostic test for VEE with negative results conducted not less than 14 days after the commencement of quarantine;
  - c. were protected from insect vectors during transportation to and from the quarantine station and during the quarantine period; and
  - d. showed no clinical sign of VEE on the day of shipment.

In addition, animals may be isolated in the importing country for seven days under official veterinary supervision. Any animal which shows a rise in temperature (taken daily) shall be subjected to a blood test for virus isolation.

#### **3.1.4.6. Article 7(d)(vi) Killing of animals**

Methods for killing of animals are compiled in (OIE, 2016a), no specific recommendation for VEEV is available.

#### **3.1.4.7. Article 7(d)(vii) Disposal of carcasses and other relevant animal by-products**

No specific recommendations for the disposal of animal carcasses and products derived from VEEV infected animals are available. The lack of information constitutes a knowledge gap.

### **3.1.5. Article 7(e) The impact of disease prevention and control measures**

#### **3.1.5.1. Article 7(e)(i) The direct and indirect costs for the affected sectors and the economy as a whole**

Some costs associated with the disposal of carcasses, if necessary, could be obtained from Extension organization (2009) (Extension, 2009). However, the lack of information constitutes a knowledge gap.

#### **3.1.5.2. Article 7(e)(ii) The societal acceptance of disease prevention and control measures**

No information has been identified regarding this item.

### 3.1.5.3. Article 7(e)(iii) The welfare of affected subpopulations of kept and wild animals

One of the measures for control is avoiding mosquito bites and this could imply stabling of animals so regulations should be followed.

Uncontrolled use of chemical insecticides could affect some animal species but strict regulations should be applied in case of need of using these compounds.

For this point, there is an important knowledge gap.

### 3.1.5.4. Article 7(e)(iv) The environment and biodiversity

Uncontrolled use of chemical insecticides could affect the environment and biodiversity but strict regulations should be applied in case of need of using these chemical insecticides. Any potential impact on the environment of the use of biocidal products beyond the intended uses, doses and target species as evaluated by ECHA is unknown.

## 3.2. Assessment according to Article 5 criteria

This section presents the results of the expert judgement on the criteria of Article 5 of the AHL about VEE (Table 2). The expert judgement was based on Individual and Collective Behavioural Aggregation (ICBA) approach described in detail in the opinion on the methodology (EFSA AHAW Panel, 2017). Experts have been provided with information of the disease fact-sheet mapped into Article 5 criteria (see supporting information, Annex A), based on that the experts indicate their Y/N or 'na' judgement on each criterion of Article 5, and the reasoning supporting their judgement.

The minimum number of judges in the judgement was 12. The expert judgement was conducted as described in the methodological opinion (EFSA AHAW Panel, 2017). For details on the interpretation of the questions see Appendix B of the methodological opinion (EFSA AHAW Panel, 2017).

**Table 2:** Outcome of the expert judgement on the Article 5 criteria for Venezuelan equine encephalitis

<b>Criteria to be met by the disease:</b>		<b>Final outcome</b>
According to AHL, a disease shall be included in the list referred to in point (b) of paragraph 1 of Article 5 if it has been assessed in accordance with Article 7 and meets all of the following criteria		
A(i)	The disease is transmissible	Y
A(ii)	Animal species are either susceptible to the disease or vectors and reservoirs thereof exist in the Union	Y
A(iii)	The disease causes negative effects on animal health or poses a risk to public health due to its zoonotic character	Y
A(iv)	Diagnostic tools are available for the disease	Y
A(v)	Risk-mitigating measures and, where relevant, surveillance of the disease are effective and proportionate to the risks posed by the disease in the Union	NC
<b>At least one criterion to be met by the disease:</b>		
In addition to the criteria set out above at points A(i)–A(v), the disease needs to fulfil at least one of the following criteria		
B(i)	The disease causes or could cause significant negative effects in the Union on animal health, or poses or could pose a significant risk to public health due to its zoonotic character	Y
B(ii)	The disease agent has developed resistance to treatments and poses a significant danger to public and/or animal health in the Union	na
B(iii)	The disease causes or could cause a significant negative economic impact affecting agriculture or aquaculture production in the Union	Y
B(iv)	The disease has the potential to generate a crisis or the disease agent could be used for the purpose of bioterrorism	Y
B(v)	The disease has or could have a significant negative impact on the environment, including biodiversity, of the Union	N

Colour code: green = consensus (Yes/No); yellow = no consensus (NC); red = not applicable (na), i.e. insufficient evidence or not relevant to judge.



### 3.2.1. Non-consensus questions

This section displays the assessment related to each criterion of Article 5 where no consensus was achieved in form of tables (Table 3). The proportion of Y, N or na answers are reported, followed by the list of different supporting views for each answer.

**Table 3:** Outcome of the expert judgement related to criterion 5 A(v)

Question		Final outcome	Response		
			Y (%)	N (%)	na (%)
A(v)	Risk-mitigating measures and, where relevant, surveillance of the disease are effective and proportionate to the risks posed by the disease in the Union	NC	75	25	0

NC: non-consensus; number of judges: 12.

#### Reasoning supporting the judgement

Supporting Yes:

- Diagnostic tools, vaccination and biosecurity measures are available.

Supporting No:

- Since the disease is not present in the EU, current measures should include import controls and movement restrictions of susceptible animals coming from infected areas. However, currently no such measures are laid down in the EU legislation.
- Both vaccines and diagnostics appear not very effective. The lack of officially or internationally recognised methods for VEEV diagnosis and the unknown Se and Sp of the available diagnostic methods could give rise to difficulties.

### 3.2.2. Outcome of the assessment of Venezuelan equine encephalitis according to criteria of Article 5(3) of the AHL on its eligibility to be listed

As from the legal text of the AHL, a disease is considered eligible to be listed as laid down in Article 5 if it fulfils all criteria of the first set from A(i) to A(v) and at least one of the second set of criteria from B(i) to B(v). According to the assessment methodology (EFSA AHAW Panel, 2017), a criterion is considered fulfilled when the outcome is 'Yes'. According to the results shown in Table 2, VEE complies with four criteria of the first set and the assessment is inconclusive on compliance with criterion 5 A(v). Therefore, it is inconclusive whether VEE can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL.

### 3.3. Assessment according to Article 9 criteria

This section presents the results of the expert judgement on the criteria of Annex IV referring to categories as in Article 9 of the AHL about VEE (Tables 4–8). The expert judgement was based on ICBA approach described in detail in the opinion on the methodology. Experts have been provided with information of the disease fact-sheet mapped into Article 9 criteria (see supporting information, Annex A), based on that the experts indicate their Y/N or 'na' judgement on each criterion of Article 9, and the reasoning supporting their judgement.

The minimum number of judges in the judgement was 12. The expert judgement was conducted as described in the methodological opinion (EFSA AHAW Panel, 2017). For details on the interpretation of the questions see Appendix B of the methodological opinion (EFSA AHAW Panel, 2017).



**Table 4:** Outcome of the expert judgement related to the criteria of Section 1 of Annex IV (category A of Article 9) for Venezuelan equine encephalitis

<b>Criteria to be met by the disease:</b> The disease needs to fulfil all of the following criteria		<b>Final outcome</b>
1	The disease is not present in the territory of the Union OR present only in exceptional cases (irregular introductions) OR present in only in a very limited part of the territory of the Union	Y
2.1	The disease is highly transmissible	N
2.2	There be possibilities of airborne or waterborne or vector-borne spread	Y
2.3	The disease affects multiple species of kept and wild animals OR single species of kept animals of economic importance	Y
2.4	The disease may result in high morbidity and significant mortality rates	Y
<b>At least one criterion to be met by the disease:</b> In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria		
3	The disease has a zoonotic potential with significant consequences on public health, including epidemic or pandemic potential OR possible significant threats to food safety	N
4	The disease has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals	Y
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	NC
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	Y
5(c)	The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it	NC
5(d)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N

Colour code: green = consensus (Yes/No), yellow = no consensus (NC).

**Table 5:** Outcome of the expert judgement related to the criteria of Section 2 of Annex IV (category B of Article 9) for Venezuelan equine encephalitis

<b>Criteria to be met by the disease:</b> The disease needs to fulfil all of the following criteria		<b>Final outcome</b>
1	The disease is present in the whole OR part of the Union territory with an endemic character AND (at the same time) several Member States or zones of the Union are free of the disease	N
2.1	The disease is moderately to highly transmissible	Y
2.2	There be possibilities of airborne or waterborne or vector-borne spread	Y
2.3	The disease affects single or multiple species	Y
2.4	The disease may result in high morbidity with in general low mortality	N
<b>At least one criterion to be met by the disease:</b> In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria		
3	The disease has a zoonotic potential with significant consequences on public health, including epidemic potential OR possible significant threats to food safety	NC
4	The disease has a significant impact on the economy of the Union, causing substantial costs, mainly related to its direct impact on the health and productivity of animals	Y
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	NC
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	Y
5(c)	The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it	NC
5(d)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N

Colour code: green = consensus (Yes/No), yellow = no consensus (NC).

**Table 6:** Outcome of the expert judgement related to the criteria of Section 3 of Annex IV (category C of Article 9) for Venezuelan equine encephalitis

<b>Criteria to be met by the disease:</b> The disease needs to fulfil all of the following criteria		<b>Final outcome</b>
1	The disease is present in the whole OR part of the Union territory with an endemic character	N
2.1	The disease is moderately to highly transmissible	Y
2.2	The disease is transmitted mainly by direct or indirect transmission	Y
2.3	The disease affects single or multiple species	Y
2.4	The disease usually does not result in high morbidity and has negligible or no mortality AND often the most observed effect of the disease is production loss	N
<b>At least one criterion to be met by the disease:</b> In addition to the criteria set out above at points 1–2.4, the disease needs to fulfil at least one of the following criteria		
3	The disease has a zoonotic potential with significant consequences on public health, or possible significant threats to food safety	Y
4	The disease has a significant impact on the economy of parts of the Union, mainly related to its direct impact on certain types of animal production systems	N
5(a)	The disease has a significant impact on society, with in particular an impact on labour markets	NC
5(b)	The disease has a significant impact on animal welfare, by causing suffering of large numbers of animals	Y
5(c)	The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it	NC
5(d)	The disease has a significant impact on a long-term effect on biodiversity or the protection of endangered species or breeds, including the possible disappearance or long-term damage to those species or breeds	N

Colour code: green = consensus (Yes/No), yellow = no consensus (NC).

**Table 7:** Outcome of the expert judgement related to the criteria of Section 4 of Annex IV (category D of Article 9) for Venezuelan equine encephalitis

<b>Criteria to be met by the disease:</b> The disease needs to fulfil all of the following criteria		<b>Final outcome</b>
D	The risk posed by the disease in question can be effectively and proportionately mitigated by measures concerning movements of animals and products in order to prevent or limit its occurrence and spread	Y
The disease fulfils criteria of Sections 1, 2, 3 or 5 of Annex IV of AHL		NC

Colour code: green = consensus (Yes/No), yellow = no consensus (NC).

**Table 8:** Outcome of the expert judgement related to the criteria of Section 5 of Annex IV (category E of Article 9) for Venezuelan equine encephalitis

<b>Diseases in category E need to fulfil criteria of Sections 1, 2 or 3 of Annex IV of AHL and/or the following:</b>		<b>Final outcome</b>
E	Surveillance of the disease is necessary for reasons relating to animal health, animal welfare, human health, the economy, society or the environment (If a disease fulfils the criteria as in Article 5, thus being eligible to be listed, consequently category E would apply.)	NC

Colour code: yellow = no consensus (NC).

### 3.3.1. Non-consensus questions

This section displays the assessment related to each criterion of Annex IV referring to the categories of Article 9 of the AHL where no consensus was achieved in form of tables (Tables 9–11). The proportion of Y, N or 'na' answers are reported, followed by the list of different supporting views for each answer.

**Table 9:** Outcome of the expert judgement related to criterion 3 of Article 9

Question	Final outcome	Response		
		Y (%)	N (%)	na (%)
3(cat.B) The disease has a zoonotic potential with significant consequences on public health, including epidemic potential OR possible significant threats to food safety	NC	83	17	0

NC: non-consensus; number of judges: 12.

#### Reasoning supporting the judgement

##### Supporting Yes:

- In general, human infection rates are extremely high, but fatalities are rare. More severe illness and higher mortality rates are observed in children and the elderly. Serious outbreaks, however, have been reported (for example, in Colombia in 1995, (Rivas et al., 1997)), and severe neurological signs have occurred.
- The disease may have epidemic potential depending on vector abundance.

##### Supporting No:

- Human cases in the last 20 years have not shown high mortality rates.
- The rate of entry is estimated to be high (EFSA AHAW Panel, 2017), but for the transmission and establishment is low, according to the outcome of the mathematical model as from the scientific opinion on vector-borne diseases (EFSA AHAW Panel, 2017) leading to an overall low to very low rate of introduction, therefore the extent of spread has not been assessed. Consequently, the exposure to humans is expected to be limited.

**Table 10:** Outcome of the expert judgement related to criterion 5(a) of Article 9

Question	Final outcome	Response		
		Y (%)	N (%)	na (%)
5(a) The disease has a significant impact on society, with in particular an impact on labour markets	NC	8	84	8

NC: non-consensus; number of judges: 12.

#### Reasoning supporting the judgement

##### Supporting Yes:

- The disease could have an impact on the society in terms of impact on the public opinion, but not on the labour market.
- Since it is a zoonosis, the safety of the people in horse stables could be affected, having an impact on society.

##### Supporting No:

- The disease could highly impact high value horse production and related markets, thus there could be a general impact on society, although this may not significantly affect the labour market.

##### Supporting na:

- The impact on the society would depend on the number of human cases that may occur in the EU, if the disease was introduced.
- Horse is a small (even of high value in some cases) production, and not many people are employed in the horse production sector.

**Table 11:** Outcome of the expert judgement related to criterion 5(c) of Article 9

Question	Final outcome	Response		
		Y (%)	N (%)	na (%)
5(c) The disease has a significant impact on the environment, due to the direct impact of the disease OR due to the measures taken to control it	NC	0	42	58

NC: non-consensus; number of judges: 12

Reasoning supporting the judgement

## Supporting No:

- The two vector species present in the EU (out of 17) do not show a significant density in the EU, thus there would be no need for a large-scale application of vector control measures leading to a major impact on the environment.
- If applied, insecticides would be used in a regulated way according to EU legislation, thus without major impact on the environment.

## Supporting na:

- No data are available on the current or potential effect of vector control measures (e.g. insecticides), and no persistence in the environment is proven. The impact on species that may be indicators of environmental pollution, like bees, is not known.

**3.3.2. Outcome of the assessment of criteria in Annex IV for Venezuelan equine encephalitis for the purpose of categorisation as in Article 9 of the AHL**

As from the legal text of the AHL, a disease is considered to fit in a certain category (A, B, C, D or E corresponding to point (a) to point (e) of Article 9(1) of the AHL) if it is eligible to be listed for Union intervention as laid down in Article 5(3) and fulfils all criteria of the first set from 1 to 2.4 and at least one of the second set of criteria from 3 to 5(d) as shown in Tables 4–8. According to the assessment methodology (EFSA AHAW Panel, 2017), a criterion is considered fulfilled when the outcome is 'Yes'.

A description of the outcome of the assessment of criteria in Annex IV for Venezuelan equine encephalitis for the purpose of categorisation as in Article 9 of the AHL is presented in Table 12.

**Table 12:** Outcome of the assessment of criteria in Annex IV for Venezuelan equine encephalitis for the purpose of categorisation as in Article 9 of the AHL

Category	Article 9 criteria										
	1° set of criteria					2° set of criteria					
	1	2.1	2.2	2.3	2.4	3	4	5a	5b	5c	5d
	Geographical distribution	Transmissibility	Routes of transmission	Multiple species	Morbidity and mortality	Zoonotic potential	Impact on economy	Impact on society	Impact on animal welfare	Impact on environment	Impact on biodiversity
A	Y	N	Y	Y	Y	N	Y	NC	Y	NC	N
B	N	Y	Y	Y	N	NC	Y	NC	Y	NC	N
C	N	Y	Y	Y	N	Y	N	NC	Y	NC	N
D	NC										
E	NC										

According to the assessment here performed, VEE complies with the following criteria of the Sections 1–5 of Annex IV of the AHL for the application of the disease prevention and control rules referred to in points (a)–(e) of Article 9(1):

- 1) To be assigned to category A, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment VEE complies with criteria 1, 2.2, 2.3 and 2.4, but not with 2.1. To be eligible for category A, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and VEE complies with criteria 4 and 5b, but not with criteria 3 and 5d and the assessment is inconclusive on compliance with criteria 5a and 5c.
- 2) To be assigned to category B, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment VEE complies with criteria 2.1, 2.2 and 2.3, but not with criteria 1 and 2.4. To be eligible for category B, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and VEE complies with criteria 4 and 5b, but not with criterion 5d and the assessment is inconclusive on compliance with criteria 3, 5a and 5c.
- 3) To be assigned to category C, a disease needs to comply with all criteria of the first set (1, 2.1–2.4) and according to the assessment VEE complies with criteria 2.1, 2.2 and 2.3, but not with criteria 1 and 2.4. To be eligible for category C, a disease needs to comply additionally with one of the criteria of the second set (3, 4, 5a–d) and VEE complies with criteria 3 and 5b, but not with criteria 4 and 5d and the assessment is inconclusive on compliance with criteria 5a and 5c.
- 4) To be assigned to category D, a disease needs to comply with criteria of Sections 1, 2, 3 or 5 of Annex IV of the AHL, for which the assessment performed for VEE is inconclusive, and with the specific criterion D of Section 4, with which VEE complies.
- 5) To be assigned to category E, a disease needs to comply with criteria of Sections 1, 2 or 3 of Annex IV of the AHL and/or the surveillance of the disease is necessary for reasons relating to animal health, animal welfare, human health, the economy, society or the environment. The latter is applicable if a disease fulfils the criteria as in Article 5, and the assessment here performed for VEE is inconclusive on compliance with the criteria as in Article 5.

### 3.4. Assessment of Article 8

This section presents the results of the assessment on the criteria of Article 8(3) of the AHL about VEE. The Article 8(3) criteria are about animal species to be listed, as it reads below:

‘3. Animal species or groups of animal species shall be added to this list if they are affected or if they pose a risk for the spread of a specific listed disease because:

- a) they are susceptible for a specific listed disease or scientific evidence indicates that such susceptibility is likely; or
- b) they are vector species or reservoirs for that disease, or scientific evidence indicates that such role is likely’.

For this reason, the assessment on Article 8 criteria is based on the evidence as extrapolated from the relevant criteria of Article 7, i.e. the ones related to susceptible and reservoir species or routes of transmission, which cover also possible role of biological or mechanical vectors.<sup>2</sup> According to the mapping, as presented in Table 5, Section 3.2 of the scientific opinion on the ad hoc methodology (EFSA AHAW Panel, 2017), the main animal species to be listed for Venezuelan equine encephalitis according to the criteria of Article 8(3) of the AHL are as displayed in Table 13.

<sup>2</sup> A vector is a living organism that transmits an infectious agent from an infected animal to a human or another animal. Vectors are frequently arthropods. Biological vectors may carry pathogens that can multiply within their bodies and be delivered to new hosts, usually by biting. In mechanical vectors the pathogens do not multiply within the vector, which usually remains infected for shorter time than in biological vectors.

**Table 13:** Main animal species to be listed for Venezuelan equine encephalitis according to criteria of Article 8 (source: data reported in Sections 3.1.1.1 and 3.1.1.6)

	Class	Order	Family	Genus/Species
Susceptible	Mammalia	Perissodactyla	Equidae	<i>Equus ferus caballus</i>
		Rodentia	Not specified	
		Lagomorpha	Leporidae	not specified
		Primates	Hominidae	<i>Homo sapiens</i>
			Cercopithecidae	<i>Macaca</i> spp.
		Artiodactyla	Suidae	<i>Sus scrofa</i>
			Bovidae	<i>Bos taurus</i> , <i>Ovis aries</i> , <i>Capra aegagrus</i>
		Carnivora	Canidae	<i>Canis lupus</i>
	Aves	not specified		
Reservoir	Mammalia	Rodentia	Cricetidae	<i>Sigmodon</i> spp., <i>Peromyscus</i> spp., <i>Oryzomys</i> spp., <i>Zygodontomys</i> spp.
			Echimyidae	<i>Proechimys</i> spp.
			Heteromyidae	<i>Heteromys</i> spp.
		Didelphimorphia	Didelphidae	<i>Didelphis marsupialis</i>
Vectors	Insecta	Diptera	Culicidae	Yellow fever mosquito ( <i>Aedes aegypti</i> )*, Asian tiger mosquito ( <i>Aedes albopictus</i> )*

\*: The mosquito species occurring in the EU are listed in <https://efsa.maps.arcgis.com/apps/MapJournal/index.html?appid=e8f840e1769b47b28fa95ac8fda0128a> (EFSA AHAW Panel, 2017).

The areas where the available information for carrying out the assessment was not considered sufficient (criteria where 'na' answers were provided) are about the potential effects of vector control measures on the environment and other vector species involved.

## 4. Conclusions

**TOR 1:** for each of those diseases an assessment, following the criteria laid down in Article 7 of the AHL, on its eligibility of being listed for Union intervention as laid down in Article 5(3) of the AHL;

- According to the assessment here performed, it is inconclusive whether VEE can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL. Eligibility of listing VEE is dependent on a decision on criterion 5 A(v).

**TOR 2a:** for each of the diseases which was found eligible to be listed for Union intervention, an assessment of its compliance with each of the criteria in Annex IV to the AHL for the purpose of categorisation of diseases in accordance with Article 9 of the AHL;

- According to the assessment here performed, since it is inconclusive whether VEE can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, then also the assessment of its compliance with the criteria as in Sections 4 and 5 of Annex IV of the AHL, for the application of the disease prevention and control rules referred to in points (d) and (e) of Article 9(1) of the AHL is inconclusive.

**TOR 2b:** for each of the diseases which was found eligible to be listed for Union intervention, a list of animal species that should be considered candidates for listing in accordance with Article 8 of the AHL.

- According to the assessment here performed, since it is inconclusive whether VEE can be considered eligible to be listed for Union intervention as laid down in Article 5(3) of the AHL, then it is also inconclusive which animal species can be considered to be listed for VEE according to Article 8(3) of the AHL.

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## Abbreviations

AHAW	EFSA Panel on Animal Health and Welfare
AHL	Animal Health Law
CDC	Centers for Disease Control and Prevention
cDNA	complementary DNA
CF	complement fixation
CFSPH	Centre for Food Security and Public Health
CNS	central nervous system
CSF	cerebrospinal fluid
ECHA	European Chemicals Agency
EEE	Eastern Equine Encephalitis
EMA	European Medicine Agency
EVD-Labnet	European expert laboratory network for emerging viral diseases
HI	haemagglutination inhibition
ICBA	Individual and Collective Behavioural Aggregation
IgM	immunoglobulin M
LD <sub>50</sub>	lethal dose, median
MLV	modified live vaccine
OIE	World Organisation for Animal Health
PHAC	Public Health Agency of Canada
PCR	polymerase chain reaction
PRN	plaque reduction neutralisation
RNA	ribonucleic acid
ToR	Terms of Reference
VEE	Venezuelan equine encephalitis
VEEV	VEE virus
WEE	Western Equine Encephalitis